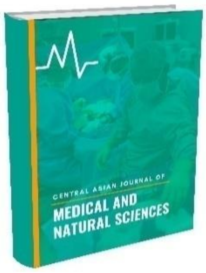
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AFFECTIVE SYMPTOMS AND STATE OF ENDOTHELIUM-DEPENDENT VASOREGULATION IN THE DYNAMICS OF IMPACT OF DIFFERENT THERAPY REGIMENS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Abstract: The progression of pulmonary hypertension and the development of chronic pulmonary heart disease in patients with bronchial asthma (BA) are closely associated with the development of endothelial dysfunction and affective symptoms.

We noted an improvement in the parameters of diastolic function of the right ventricle, mean pulmonary arterial pressure, the level of stable metabolites of nitric oxide, endothelium-dependent vasoregulation, and psycho-emotional status in patients with bronchial asthma complicated with chronic pulmonary heart, occurring after complex treatment using bischofite and nebivalol on the background of standard therapy.

Key words: bronchial asthma, bronchial asthma, chronic pulmonary heart, endothelium-dependent vasoregulation, affective symptoms, respiratory function, nebivalol, bischofite.

Bronchial asthma (BA) is one of the most common diseases on all continents. According to experts, about 235 million people already suffer from this disease and by 2025, given the rapidly increasing urbanization among the population, the prevalence in the world may increase by another 100 million people (Masoli M. et al., 2014). In Russia, the incidence rate of bronchial asthma ranges from 0 to 2.5%, whereas in developed countries it is usually higher than 6%. Mortality from bronchial asthma continues to remain at a fairly high level in Russia: more than 10 per 100 thousand cases, which exceeds several times the mortality rates in Europe and North America (Emelyanov A.V. et al., 2012; Kurbacheva O.M. et al., 2012; Ilyina N.I. et al., 2013; Masoli M. et al., 2014). It is the complete control of the symptoms of the disease that helps to successfully manage patients with asthma and in the long term helps to reduce the number of exacerbations, as well as adverse outcomes of bronchial asthma. (GINA, 2014) [4,9]. Periodic attacks of the disease are accompanied by hypoxemia of varying duration, which is often the main cause of arterial vasoconstriction [Avdeev S.N., 2009; Strutynsky A.B., 2009; Leuchte H.H., 2006]. Chronic inflammation in the respiratory tract underlying AD may

acquire systemic features, which contributes to the rapid progression of ventilation and hemodynamic disorders [BroideD.H., 2013] [6].

The role of damage to the endothelium of the pulmonary vessels in the change of pulmonary circulation in AD has already been reliably proven. Under the influence of chronic inflammation and hypoxemia observed in AD, the endothelium is damaged, the balance of production of regulatory substances is disturbed, which provokes an inflammatory-proliferative reaction in intima and adventitia of pulmonary vessels and leads to a change in the vascular bed and the development of secondary chronic vasoconstriction [7,10].

Pulmonary hypertension (PH) is defined as a group of diseases characterized by progressive pulmonary vascular resistance, which leads to right ventricular failure and premature death [1]. Data on the prevalence of LH are heterogeneous due to the significant number of nosological forms attributed to this syndrome. Nevertheless, LH ranks third, after coronary heart disease (CHD) and arterial hypertension (AH), among cardiovascular pathology in people over the age of 50. [8]. According to the definition of the WHO Committee of Experts, chronic pulmonary heart disease (CHL) is hypertrophy or a combination of hypertrophy and dilatation of the right ventricle, arising from diseases affecting the structure or function of the lungs, or both at the same time. CHL develops in chronic obstructive pulmonary diseases complicated by the development of pulmonary hypertension. One of the most difficult clinical tasks is the treatment of decompensated CHL, which is largely explained by the complexity of the pathogenesis and underlying pulmonary hypertension. [2]

In recent years, Uzbekistan has seen an increase in the prevalence and mortality from lung diseases complicated by chronic pulmonary heart disease. To optimize early diagnosis, adequate prevention and treatment of CHL, it is necessary to clarify the factors leading to its development and aggravating its course. [5]. Chronic pulmonary heart disease (CHL) is one of the important problems of modern medicine. Despite the fact that the problem of CHL has been dealt with for a long time, there are many questions in understanding the mechanisms of formation and progression of this pathology. The pulmonary heart should be understood as the whole complex of hemodynamic disorders (primarily secondary pulmonary hypertension), developing as a result of diseases of the bronchopulmonary apparatus and manifested, at the final stage, by irreversible morphological changes in the right ventricle of the heart, with the development of progressive circulatory insufficiency.[3]

The purpose of the study. To study the state of the pancreatic diastolic function, pulmonary hemodynamics and vasoregulatory function of the peripheral vascular endothelium, the relationship of mental disorders in patients with bronchial asthma in the dynamics of complex treatment**.**

Materials and methods of research. 43 patients were examined (age 51.2± 3.5 years, disease experience 11.3±3.2 years), in whom the disease was complicated by the development of LH with the level of mean pulmonary arterial pressure (LADsr) more than 25 mmHg. 37 patients with BA (age 57.8±3.2 years, disease experience 15.7± 3.8 years), in whom the disease was complicated by GPH (the thickness of the anterior wall of the pancreas of the heart > 5 mm, with an anterior-posterior size of the pancreas greater than 2.5 cm) and 23 healthy individuals (ZL) were also examined.

The patients according to the treatment method were randomized and divided into 3 subgroups, respectively: subgroup A - 11 patients with AD with GPH (1a) and 13 patients with AD with LH (2a) received standard therapy (CT) according to the international recommendations of GINA (2011); subgroup B - 14 patients with AD with GPH (1b) and 16 patients with AD with LH (2b) on the background of CT received highly selective beta-blockers of the III generation-nebivalol (A) b a dose of 2.5-5 mg per day and bischofite electrophoresis (EB).; subgroup B - 12 patients with AD with GPH (1b) and 14 patients with AD with LH (2b), in whom standard therapy was combined with EB.

Bischofite was performed in the form of electrophoresis daily, for a course of 10 infusions. The effectiveness of therapy regimens was evaluated in dynamics on the 10th day of therapy.

The psychoemotional status of patients was assessed on the basis of psychological testing using the Spielberger test for the det.

Research results and discussion. The dominance of anxiety affect in the personality structure is confirmed by the results of psychometric analysis using the Spielberger method using the scale of reactive anxiety and personal anxiety. In all patients with AD, high anxiety was found as a stable personality trait. According to the Spielberger scale, patients with AD with GPH and LH showed a significant increase in personal anxiety by 38.6 and 32.5%, and especially reactive anxiety by 40.4 and 38.2%, respectively (compared with healthy individuals). The data obtained by us in a subgroup of patients with BA complicated with GPH showed that the level of reactive anxiety and the level of personal anxiety is higher compared to patients with BA complicated with LV.

The results of the study found that in patients with BA complicated by CHL, there is an imbalance in the levels of stable metabolites of nitric oxide (CMNO) in the blood plasma and a decrease in the ability of PA vessels to active endothelium-dependent vasodilation. Thus, the analysis of the results of samples with reactive hyperemia showed that in patients with CHL, the maximum systolic blood flow rate was significantly reduced and correlated with the severity of the disease. In patients with BA complicated by CHLC, the MSS indicators in response to CP are reduced, compared with the indicators of healthy individuals by 32.9 and 19.2%, respectively, the ICS is increased by 38.6 and 28.0%. In parallel with the deterioration of VSL and endothelium-dependent vasodilation, there is a violation of the diastolic function of the pancreas of the heart.

It should be noted that in patients with BA complicated by CHL, changes in the structure of the filling of the pancreas in the diastole were significantly pronounced Note: in the numerator, the indicators were before treatment, in the denominator - after treatment (**$p<0.005$ and *$p<0.05$ the reliability of the difference with the indicators before treatment).

The decrease in filling indices we found in the early diastole is associated with a violation of relaxation of the hypertrophied myocardium of the pancreas of the heart, as a result of which the decrease in intraventricular filling slows down and the AF increases.

When using bischofit, as well as nebivalol and bischofit against the background of CT in patients with BA complicated by CHL, there was not only a decrease in LADsr, DD, but also an increase in CMNO and endothelium-dependent vasodilation. The maximum systolic rate after the compression test increased by 6.7 and 7.6% ($p<0.05$). A decrease in the circulatory resistance index of vessels was determined - by 6.9 and 7.2% ($p<0.05$). Positive changes were observed in the parameters of the diastolic function of the right ventricle. During therapy with the use of nebivalol and bischofite in patients with AD complicated by GPH and LH, there was a significant decrease in indicators: the time of isovolumic relaxation, respectively, by 9.7 and 10.5%, the time of slowing down the maximum rate of early diastolic filling - by 6.6 and 7.3%, atrial filling fractions - by 11.8 and 13.9%, LADsr - by 13.1 and 15.7%. Against the background of the therapy, the E/A ratio increased by 11.5 and 12.4%, respectively ($p<0.05$) and an increase in CMNO by 9.7 and 10.6%. Affective symptoms decreased: RT by 5.1%, LT by 7.1%.

Electrophoresis with bischofite on the background of CT in patients with AD led to an increase in the maximum systolic velocity after compression test by 5.9 and 5.2% and a decrease in the circulatory resistance index of vessels - by 6.2 and 6.7%, respectively ($p<0.05$). The following indicators were found to decrease: the time of isovolumic relaxation, respectively, by 4.6 and 5.1%, the time of deceleration of the maximum rate of early diastolic filling - by 3.8 and 4.1%, the fraction of atrial filling - by 8.3 and 9.9%, LADsr - by 8.7 and 9.5% ($p<0.05$). The ratio of early and late diastolic filling increased, respectively, by 7.7 and 8.3% ($p<0.05$) and an increase in CMNO by 6.1 and 8.1%. Affective symptoms decreased: RT by 4.8, LT - by 5.4%.

The obtained data allowed us to state a more pronounced improvement in the indicators of CMNO, ESVD, VSL, diastolic function of the pancreas of the heart and affective symptoms in the dynamics of the regimens of complex therapy with the use of nebivalol and electrophoresis with bischofite in patients with BA with LH, compared with patients with BA complicated by GPH.

The results of the study indicated that the standard therapy regimens had no effect on changes in the parameters of the diastolic function of the pancreas of the heart and the level of mean pulmonary arterial pressure.

As a result of the study, the vasodilating effect of bischofit and nebivalol was confirmed, which was manifested by a decrease in pulmonary arterial pressure and an improvement in the indicators of the diastolic function of the pancreas of the heart.

Studies have shown that before the start of treatment, an increase in affective symptoms, a decrease in AF, SMNO and changes in the ability of vessels to actively vasodilate are parallel to violations of the structure of the filling of the pancreas in the diastole. These changes are significantly pronounced in patients with AD with GPH compared with the indicators of patients with AD with LH. Mutual aggravation and progression of disorders of peripheral and central hemodynamics is based on the commonality of some links of pathogenesis: the development of disorders of AFL and CMNO level, pulmonary-cardiac microcirculation and pulmonary hypertension (Vermeire P, Pride N.B et al., 2001; Fisnman A.P., 2004). The progression of LH and the development of chronic pulmonary heart in patients, We noted an improvement in the parameters of diastolic function of the right ventricle, mean pulmonary arterial pressure, CMNO level, ESVD and affective symptoms in patients with BA complicated by CHLC, occurring after complex treatment with bischofit and nebivalol against the background of CT.

Conclusions:

1. The hemodynamic load on the right parts of the heart, an increase in the size of the pancreas and the thickness of the pancreas in patients with AD directly depend on the severity of systemic endothelial dysfunction and the duration of the disease.
2. In bronchial asthma, a decrease in the ability of peripheral vessels to actively dilate blood vessels positively correlates with the state of the diastolic function of the pancreas of the heart and the tone of the pulmonary vessels necessary for normal gas exchange of lung tissue.
3. Preparations of highly selective β1-adrenoblockers - nebivalol and the natural drug bischofit reduce endothelial dysfunction, remodeling of pulmonary vessels and improve the function of the right parts of the heart, an increase in the degree of endothelium-dependent vasodilation and a significant decrease in systolic blood pressure in the pulmonary artery and improve affective symptoms in patients with asthma complicated by varying degrees of CL

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